REGULAR MEETING

CALIFORNIA AIR RESOURCES BOARD

SCIENTIFIC REVIEW PANEL

ORIGINAL

San Francisco Conference Center

Suite E

1240 OLD BAYSHORE HIGHWAY

BURLINGAME, CALIFORNIA

TUESDAY, OCTOBER 22, 1991

9:10 A.M.

Reported By: Clara Mae Mathis,
CSR No. 2832

MEMBERS PRESENT

Dr. James Pitts, Chairman
Dr. Charles Becker
Dr. Craig Byrus
Dr. John Froines
Dr. Stanton Glanz
Dr. Hanspeter Witschi

MEMBERS ABSENT

Dr. James N. Seiber

STAFF PARTICIPATING

Genevieve Shiroma
Dr. Joan Denton

OTHERS PARTICIPATING

Dr. George V. Alexeeff
Department of Health Services

Dr. Stanley Dawson
Office of Environmental Health Hazard Assessment

I N D E X

P R O C E E D I N G S

--o0o--

CHAIRMAN PITTS: We will officially declare this meeting, which has been going on for at least ten minutes, we will officially declare it operative, as it were, and welcome the panel members that are here, and the staff, the audience.

And the first item of business will be a discussion, a brief discussion and review, of certain relevant actions that took place at the Board hearing on perc last Thursday, and Genevieve Shiroma will present the material open for discussion.

MS. SHIROMA: Thank you, Dr. Pitts.

Just very briefly, we had a very lively Board hearing two weeks ago, and as I mentioned earlier, we want to thank Dr. Froines for help on the job and with our SVP deliberations in adopting perchloroethylene.

The Board did a number of things in adopting perchloroethylene. And they voted unamimously to adopt. perchloroethylene as a contaminant. That was very clearly done. They also accepted the range of risk that was included in the scientific material. They did not accept the best value; however, they did not reject it either.

But they instructed the staff to hold a workshop for the ARB, the Office of Environmental Health Hazard Assessment, and at least one member of the SRP. They proposed to hold a workshop on the best value to work at additional

perchloroethylene and to have a dialogue with the various interested parties on that, and to report back on that within four months to the Board, and George Alexeeff is working with us on that workshop.

(Dr. Craig Byrus arrived at the meeting.)

The Board expressed strongly and felt strongly that the it was best to continue with the best science with the kind of work that we all have been doing. There was no question about that.

The Board did express concerns regarding the proper use of the risk assessment value in risk management on the one hand. There were certain statements being made about the risk assessments, the risk management, the use of the risk values that come out of this process. They were concerned about this given that there are, as we all know, these are inherent in certain risk assessment technologies.

The Board felt they needed to take a leadership role in providing the necessary information regarding proper use of the risk assessment values and in terms of risk management. We think that you're aware what we are talking about is the decisions being made whether it's at the local level or at the state level regarding control requirements, or permanent requirements, or notifications to the public on hot-spot facilities.

The Board directed the executive officer to work with the

Scientific Review Panel, the Office of Environmental Health Hazard Assessment, the public, and the industry on looking at the process of using the risk values in risk management to develop recommendations on the appropriate tools in how to interpret those risk values.

We are to report back to the Board in six months on our progress on this endeavor. And so shortly the staff --

DR. FROINES: Would you say that part again. I missed something.

CHAIRMAN PITTS: Go through the whole thing in terms of process.

MS. SHIROMA: What's meant there is that the Board wants the Air Resources Board staff executive officer to start a dialogue with you folks, with industry, the districts, the public, the Office of Environmental Health Hazards Assessments in looking at how those risk values are used. Is that the appropriate use today in the terms of making a decision about whether or not or to apply it in order to control it.

To start that dialogue, as far as how are those decisions being made? And should there be some discussion about whether or not there are some alternatives as far as how those decisions are being made in risk management. So it's to start that discussion. We're not trying to predetermine what the outcome is. Many people out there know how to go about making decisions.

One idea we had was to start with a focused seminar or conference in early 1992. We would bring in a lot of the experts, a lot of people who are familiar with whether it's -- how one goes about making a decision and start a discussion. We were discussing earlier that right now the districts are in many cases saying that if you are over a certain risk level, you may or may not receive your permit. It's a very simplified approach at this point.

The Board wants to hear back from us on in six months on our progress. I'm sorry. From the staff. I'm sorry. From the Air Resources Board staff. And in our work with this Scientific Review Panel and all on others.

CHAIRMAN PITTS: Excuse me. I need to get that again clear in my mind. Is that going to be related to the actions that the Board will be taking in the risk-management context after the SRP has gone through this whole procedure?

MS. SHIROMA: That's right. There was a clear signal of a separation between the risk assessment and continuing with the best science, the best methodology available to you, continue with that work. It's that phase where you have finished your work, made your recommendation, your assessment of the range of risk, how should those pieces of information can be used in risk management. How should those pieces of information be used by the air pollution control decision, the State Board in making control decisions?

It is a very clear signal. They are not telling you to make changes in the way you approach the findings; what they are saying is that you should take a look at -- once we have those risk values what do the the risk managers do with those values?

CHAIRMAN PITTS: I'm not through yet. This is a very, very key point, because I think historically -- stop if me if I'm incorrect -- basically, this is the first time that the Air Resources -- I'm not drawing a judgment value on this. I'm just trying to historically go through this.

It's the first time that the Board has not accepted a unit risk best value that has come through the entire process, scientific process, and used that. Is that right? At least accepted that value.

Because we're saying if they did not accept the value of whatever it was -- 54, the number was.

MS. SHIROMA: It's the first time that they have made this kind of evaluation. I may say they did not accept the value, nor did they reject. It they asked the staff, the Air Resources staff, the Office of Environmental Health Hazards staff along, with the SRP representation, to go back and hold one more public dialogue with the interested industries and public, come back to the Board with the recommendations.

So what they have essentially done is put that best value on hold until we have this one additional public dialogue. Now in the past, the Panel would include a range of risk.

CHAIRMAN PITTS: We always have. That's correct.

MS. SHIROMA: It's really only recently that the Health staff has started to also include a best value, so there has been some evolution in the process.

That would be taken to the Board, the range of risk. The Health staff began to include a best value. We have now come to the point where perchloroethylene, where they have asked us to go back, have that one more dialogue, come back to the Board with a recommendation on what that best value would be.

CHAIRMAN PITTS: Now, what do we do on formaldehyde today?

MS. SHIROMA: Oh formaldehyde today --

CHAIRMAN PITTS: Clearly we will have a range. The range has been there for some years, and the best value has been around for seven years, hasn't it?

DR. GLANZ: Methylene choride was the first one.

MS. SHIROMA: Methylene chloride, nickel TCE, chloroform, which only lasts two years.

DR. GLANZ: Two years. As I recall, the best value didn't originate with the staff. I kind of remember the Panel wanting that.

CHAIRMAN PITTS: That's right.

DR. GLANZ: And I feel quite strongly that we have a responsibility to come up with best value number now. What the ARB decides to do with it is sort of their business, but I think

we should, in these reports, include the range and the best value. I think that it would be irresponsible not to.

MS. SHIROMA: And the Board was not asking for anything differently. They were basically saying continue in providing that information.

DR. GLANZ: Now was there -- I talked to Bill Lockett about this a little bit a couple of days ago, and we have established the streamlined process. But was perchloroethylene something that was sort of in a transition period where there weren't as many public workshops, public meetings, as we have under this process?

MS. SHIROMA: That's correct. Perchloroethylene was one of the last of that.

DR. GLANZ: Okay. I think that that's a very important point in terms of going back and having this additional public meeting, and I would personally like to construe that as a peroration in the system due to the fact that through the transition, a public meeting wasn't held rather than setting a precedent for changing the procedures we have put in place.

MS. SHIROMA: Right. The Board indicated this was setting a precedent for future compounds, because, as you say, we have streamlined the principles today where the workshop is incorporated into the streamlining process.

CHAIRMAN PITTS: I have another question. It may have occurred to some of you, but it has occurred to me who -- on

what basis, what scientific basis, what science, or how is ultimately the final value -- what the science is going to be behind the final value for perc? Will the science be -- will that value be determined -- who will determine the science upon which the Board finally makes a decision that the number isn't 54; it's ten.

I thought the Panel was supposed to be our science input, and that was risk assessment. And I sort of see -- I'm not sure how that's going to happen.

DR. FROINES: Let me comment on that. The Board was concerned, and when the meeting began, the Board was more than concerned. They were hostile and --

CHAIRMAN PITTS: To whom?

DR. FROINES: To everyone. They felt they had been lobbied very hard by a lot of different people, and since they hadn't heard the other side, in a certain sense there was a lot of tension in the room excluding the number of people who were in the audience. So the Board had been told basically by a number of people that there had not been an adequate participation and a workshop, and they in a sense seized on that, and that was then later discussed by the fellow from the -- Paul Kammer, who raised it.

And so it was an issue before the Board. And so we had a lot of discussion about that about how science is done, and about how laws are done, and that sort of thing, and so on, and

so forth, but basically that was a sticking point. It was a sticky perception that people had.

So what happened was basically what the Air Resources Board did -- Genevieve, is entirely correct -- was not rejected, the best number. To simply recognize that perchloroethylene was a difficult document. It was complicated. There were a lot of uncertainties, and they simply said, "Go back. Take a look. If you come up with same number as you did before, fine. Bring it back to us."

And basically implying that they would then adopt that.

"If you change your mind, bring us back another number."

The issue isn't so much the number as it is the process, and it's the process that they were concerned about.

And so let me stop. And I want to come back to this risk-management issue in a few minutes, but that's really what was going on.

MS. SHIROMA: So, Dr. Pitts, processwise our plan is continue with the same methodology in that the best values are developed by the health staff, George and his staff. They are reviewed by the lead SRP member.

And one thing that we could take a look at is what we're getting is butadiene and the other compounds. In going back and developing those values, George came before us to discuss this with you. And before that they moved into the administrative stage.

And I think the Board wants to go back, and we go back to the Board in very short order, essentially to hold that workshop with the public, George's staff, looking at where there is additional data, new data.

DR. GLANZ: Well, again, I think again I see this as a transition, a problem that was created by the change in procedures that we're using, and I think it's important that the SRP maintain control over that number in terms of what gets recommended to the Board. So what I would suggest we do with this -- and again because it's a transitional problem -- is you have your work shop. John is there.

But I think it should come back to us before it goes back to the Board and give us a chance to either amend our previous recommendation or to say, "Well, we're going to stick with the previous recommendation." So it's very clear that a group can't come in after the fact and sort of sidestep the process here.

DR. FROINES: I think there is something that I talked to the Board about and they accepted wholeheartedly and with enthusiasm, and that's that this Panel's role is to be a quality control-quality assurance aspect of this process as a scientific matter. Therefore, two things: (1) we are really not going to get into a kind of a chin-to-chin dialogue and debate these issues with industry, or environmental groups, or whoever.

Our job is George should organize the workshop. Anybody from the panel who chooses to attend should do so. But then it

incumbent on George to bring back the results of that workshop to us so we can continue to play that quality control role. So then we go forward.

But we are not now being asked to become kind of the third participant in the ring. We are to continue to play our role as we have played it, and therefore it's George's responsibility to carry out the workshop.

CHAIRMAN PITTS: Dr. Becker.

DR. BECKER: See, Genevieve, that's the kind of thing that's confusing to me. Because if, at the time, I participated in this process, I don't believe that any of our decisions was made on the management process. I have never heard that discussion.

MS. SHIROMA: That's correct.

DR. BECKER: So now I will agree with what John said. I'm uncomfortable about the management side of it, because you know, track record on that, we have no input.

MS. SHIROMA: And I should emphasize you're not being asked to specifically start to make risk-management decisions. In fact, quite the opposite. The Board was very clear that the science that you're using, the methodology that you're using, that's your purview, and you should continue with that.

It's up to the Board staff, executive officer, working with the various groups involved -- the health folks, the industry, and public as well as with your link to the standards.

It's up to staff to work in developing those tools as to how to make the decision on whether or not to issue a permit.

DR. FROINES: I want to just say this: I want to be as stable and strong as possible. It is not the role of this Panel to be involved in the risk-management process, (1).

Secondly, it seems to me that it is this Panel should be precisely precluded from being part of the risk-management process because the decisions about how much cancer one is willing to accept in a society is a social decision. It should be made, not by a small body of scientists who think they have some measure of truth around risk-assessment numbers. It should be made by the public; it should be made by affected industries, by scientists, by environmentalists, by the public, by government agencies.

The social decision about what one is prepared to accept is a decision that should not be made, as far as I'm concerned, by nine scientists. It's out of the scope of our role.

I think our role is to do the very best science and precisely be precluded from the risk-management phase of the concept. It doesn't mean that we wouldn't necessary participate in the risk-management process under a difference guise, but it means that this process, it seems to me, has to be separate.

CHAIRMAN PITTS: I would just say for the record that is what actually was the whole theory and premise upon which this whole 1807 was founded and has been -- I guess John and I are

the original charter members of this -- has been the way it's been operating through the years. At no the time have we ever felt we were part of this management.

But there is a difference -- there is a difference -- in this step here that I was referring to in the risk-assessment phase, because we have been asked for the first time as a panel to take a compound which has not -- benzene is another case. We had a set of rules. If they want to come back on benzene, the following things have to be done. It has to be covered with literature.

This is different. It's qualitively different. I'm not objecting to this. I'm not saying it's wrong. I'm only saying this is different, and I want to be sure that the risk assessment is, in fact, handled in the way we expect to see it handled. And I agree with Stan.

One more thing. Let me ask this question. I'll ask the question and see what happens. Formaldehyde is a very controversial area. There is a lot of pressure on formaldehyde. I think we have just begun to see this. I understand a lot.

Let us suppose we come to a value, whatever the number is. Seven is it? Something times ten to the minus. The wide range is a factor of 40 or more than 40. Now, what happens if we have in the risk management phase -- is there a possibility or probability that in public testimony -- there will be a public testimony? There will be -- it won't be the same as

perc. It won't be of that intensity or maybe it will.

We'll then go back again and go through another process in which we say, "Okay. Here's the range, and here's the best value. We have a lot of information from industry." And we want to go back and go through the same process. I think that's significantly different from what we have ever done in the past.

MS. SHIROMA: Let me clarify. George?

DR. ALEXEEFF: My name is George Alexeeff, the Office of Environmental Health Hazard Assessment.

CHAIRMAN PITTS: OEHHA.

DR. ALEXEEFF: I want to essentially make a comment. It refers to what Dr. Pitts is saying. It's an extension of what Dr. Glanz is saying.

We would add the perchloroethylene as -- I would say as an exception in the system, and although Genevieve focused on the risk-management aspects of it, I think the real reasons that we're looking at it again are twofold. One is there was an initial indication that we were going to have a workshop.

No. 2, there was only a ten-day comment period from our final document, and because the actual choice of the number has such a potential impact, I think the Board just wanted to make sure that the ten-day comment period with the absence of a workshop that we were sure.

With formaldehyde we have had the workshop, and we have had a 30-day comment period. It's not at all the same issue as

with perchloroethylene.

We have dealt with a lot of controversial chemicals, and I think simply that we felt that although the procedure we used was legally correct, that it really did not provide enough public access whereas in formaldehyde we have provided as much as we can.

CHAIRMAN PITTS: That's not according to what Chevron said in the first public comments.

DR. GLANZ: They always say that.

CHAIRMAN PITTS: I don't understand that. I don't understand that.

DR. GLANZ: Well, I'd like to make a suggestion. Again, I think we are dealing with a special case here because of this transition, and I think that it would be worthwhile -- I think it might be useful for the Chair to send a letter to Jan Sharpless saying that the Panel recognizes that there are some special circumstances surrounding perchloroethylene because of the transition to the new process, that there was not a public workshop, and therefore, we are quite happy to have the staff go ahead and hold the workshop and then come back to the Panel with just that one point for final clarification. And then it can be sent back to the Board.

And say that we don't anticipate that this is establishing a precedent as long as the new procedures are followed. We would hope once something gets out of here, it's

gone.

DR. FROINES: But I don't think that -- maybe I should take a minute and tell you what the real change is so you understand what's being discussed. Because I want to speak as strongly as possible that there was never an issue raised whatsoever about this Panel having to modify its process with respect to the risk assessment number. I mean that never even came up.

So we are having a discussion here that a has a little bit of unreality to it. Let me tell you what did come up, because I brought it up. It's the underlying issue which nobody has described yet.

With perchloroethylene, there was a number of risk values. There was the value that George came up with that was represented -- that was based on assuming a certain percentage of metabolism of perchloroethylene which represented the most probable upwardbound. Upwardbound.

Now, George uses the most upwardbound because that's what his cancer policy has told him to do over the last0five years. He operates on the basis of conservatism. If somebody said, "George, always comes back with the life investment," he would do that, but the policy he operates by is, for the most part, coming in with conservative approaches. Fair?

Now, there was a lower number which was assuming a metabolism of around five percent that was the m▒st probable

number, the best average if you will. And then there were some numbers that were lower down around two percent that I think the data that they're derived from are such that they're not acceptable as a matter of science. They are based on incomplete metabolism.

Okay. Now, here's the issue. Here's the issue. So let's forget the 73 percent metabolism and the two percent metabolism, but let's assume that we have two reasonable numbers. One is a probable upwardbound, and one is a best estimate.

Now, it's those two numbers that I think the Board, and the staff, and the people who do risk estimate are going to have to look at when they get into the risk-management phase, because they're going to have to decide, given the uncertainty -- and there are a lot of your uncertainties with perchloroethylene -- given the uncertainties with perchloroethylene, what is the most appropriate value to use for purposes of risk management?

And it could be the most probable upwardbound, and it could be the best estimate. But the attempt the risk manager is going to have to do is to factor in how do you address scientific uncertainty? How do you address cost, and how do you address control technology, and all those things.

So what's being said is that it may be that the risk manager may accept a value different from what we think is the best value, because the best value that we came up with is the

probable upward best. But in a certain sense, that may not be the best value from the standpoint of risk management.

And if that -- if the attempt on the part of the risk manager to do a much more sophisticated evaluation of the data than has ever happened before. So what we're talking about is the risk-management process should become a more sophisticated process and not simply be the, quote, bright line, the number that we come down with is the bright line that the South Coast Air Quality Management District says they're going to go with which means we, in effect, are making a risk-management decision. We are.

And we ought to understand that when we see what South Coast is doing. So my point is that what the risk manager should do is not necessarily accept our best value. But it becomes one of the values. It becomes part of risk-management process.

And that's what the issue is really about. It has nothing to do with this Panel changing it's point of view; it has to do with how do we improve the risk-management phase to make it a better product as opposed to risk assessment?

DR. ALEXEEFF: I'd like to make one comment with regard to the workshop. I think you have put it perfectly, Dr. Froines, and I think the issue I would hope we might be discussing at the workshop is the relative merits of the five and 25 or a potential other number somewhere in between.

And if there is some change that's made, if for example, after reviewing the data, we decide that, let's say, five percent is really the better value to go with, and then my thought would be we would prepare documentation of that and send it to the Panel again for the review before public comment again, a ten-day period or whatever is required. It would go to the Panel, and I guess without public comment. It would simply be -- it would involve public comment. It would simply be a ten-day period for the Panel to review it. And then we would meet on it as a panel. We would have to consider if there is a panel or not.

DR. FROINES: The key point that your determination should not change because of the subsequent risk-management phase.

MS. SHIROMA: Exactly. Exactly.

DR. FROINES: We should make that the law for the way we operate.

DR. ALEXEEFF: The focus has to be strictly on that metabolism range. What do we know about it? How do we get them? Is there a better way?

DR. BECKER: I'd like to endorse Stan's suggestion. I had a chance to talk to Jan Sharpless. There was some question whether we would all appear at that session. I had to teach students on that day and couldn't.

I think that what happens is the perception of a little

about the bit of arrogance that we were trying to do something that was never the intention of anyone around the Board. And so I think perhaps just a gentle letter saying that we want any data that we have which is reasonable for us to consider.

We're here not put up a barrier for any scientific information. I think that's what they wanted to hear from us, and I think if we took a little bit of time and sent a letter from our Chair saying that we're here. We're here not setting a barrier of ten days or forcing this issue.

Because I think there was a perception that which in my experience has not been a reality. It seems like there were extenuating circumstances. A carefully crafted letter which would be a little bit humble, which, in fact, I think is what the Panel, in my experience of the Panel and all the documents really have been such that we were interested in having more information. We are open, not closed.

I think that would go a long way to just take some of the energy out of this.

DR. FROINES: I agree with that, but I want to state something, that I think it's important for us all to recognize. And I was joking when I said about the 300 people sitting behind me when I was presenting it.

But what's happened now -- we didn't do anything wrong. That shouldn't have even been an issue. What happened was that there were a lot of industry people who went out and garnered a

lot -- went out and raised the flag about people are going out of business and said industries were going to die, and on and on. You saw all the letters that came through. There were hundreds of them.

And so there was an immense politicization, if you will, of the process. And there were 300 people there, and it was a very tense situation. And the Board was responding to that.

And I think there's something that we have to be very clear about. I think that we have to be clear (1) that we are completely open to any and all information that is timely and scientifically appropriate.

And secondly, I think we should also be clear that we don't intend to bow to the sort of politics of the situation because we don't want -- if the signal goes out that the Panel now will change what it does, and OEHHA will change what it does, and the Air Resources Board staff will change what they do because of the political pressure generated around perchloroethylene.

Then we have taken a step down the wrong road, as far as I'm concerned. And we want to be careful that we make it clear that this Panel is going to continue to function as it has within the process.

DR. GLANZ: I totally agree with that. I have been embroiled in a couple of controversies in San Francisco having to do with zoning. And I can tell with you when you're very

unhappy about something, and you have been deprived of what you perceive as your chance to get up and say your piece, people going ballistic.

And I think what happened here is there was in the transition, there was -- this workshop didn't get held, and I think that people reacted very, very negatively to that. And I think we should fix it.

But I think it's important, going along with what you're saying, John, to say that this coming back to us, is to fix a procedural error that was made in the transition to the new process. And so, you know -- and to make that clear, and so we're not establishing a precedent. We are not bound by political pressure. We are giving people an opportunity to be heard that they were inadvertantly deprived of because of the change that went through the channel.

CHAIRMAN PITTS: I think what I will do here, we have one person, I believe, in Washington, and we need to get onto formaldehyde. I don't want to break this up.

One last comment here. Just one last comment that again I agree. It is agreed, then, that we should write a letter along the lines and we will draft such a letter?

DR. BECKER: And I would like to suggest that what George had to say, this was an exception. This Panel is getting involved in many compounds. This was this perception which was not our intent, and we are going forward with change, no

scientific compromise. That's a strong point that we should make.

CHAIRMAN PITTS: It was all in the first hearing. It's in the record. The Panel expressed its concern. There was only ten days between the time that went out, exactly that. We expressed our concern on the record that there was not a workshop. So that was all said back last June. I agree in a pleasant way we agreed. In fact, we had some discussion.

Okay. One last little thing now. As I read the letter from Chevron, in Part C it says here -- Part C. This is on formaldehyde. I'm concerned that we register what happened.

It says the EPA -- in Part II it says.

(Reading)

The ARB should be aware that EPA is currently revising their estimate of unit risk for formaldehyde's carcinogenic potency. The EPA's best estimate, quote-unquote is approximately two orders of magnitude lower than the DHS's best estimate. -- developed in the rat. Dah, dah, dah, dah -- Why do the experts disagree?

(End of reading)

And then in the response it says,

(Reading)

Studies that observed less cancer are more consistent with the revised best estimate which is well below the revised top of the range."

(End of reading)

It seems to me, as I see it, that's sort of a similar scenario here where you have a wide range. You have the best estimate.

And then you have the so-called best estimate. After this if a number is picked today, will we again go through a process, or can we expect to go through a process in which we discuss -- the Board decides well, there is a high level, the conservative value. There is a best estimate. We will just go back and look at this.

And my question would be, then, in that case, will there be there another meeting? Will there be a reexamination? Will there be another best estimate come back to the -- and then also what that leads to, by the way, is a better understanding of what Chuck was saying. I think we need to understand carefully what the process is going to be. We have been in a transition stage. I agree with that. But I'm not sure I see where the transition is ultimately leading to.

DR. GLANZ: that's why I think we should treat this as a procedural matter.

CHAIRMAN PITTS: That's what I said. That's exactly my point.

DR. GLANZ: We do have -- let me make one more comment. You all have in your information sent to you, because we discussed this with the chief of staff, you know, John and I

did, last Wednesday with the industry representative.

This is a Scientific Review Panel process for evaluation and response to submittal of new scientific information as evidence for review of CAC's risk assessment. In other words, this would be the benzene.

Remember, we went through this in '89. And we said we have a whole set of criteria: screening submittals, for example. It has to be peer-reviewed, new evidence, and the change is supposed to be -- it seems we are sort of saying here again, too, what we really need -- and I would hope the Panel would agree and perhaps the Board does -- a statement of this not for a review for one which has already been a CAC declared in the past, but a process clearly laid out now that will define where this transition is going to lead us. And then we will have it in black and white, and it will be publicly circulated so all the players -- industry -- understand what the process is. Is there any problem with that?

Just redo it. We can redo it. Have a draft. There is no hurry. We will do it right. And we will get back with the Board or get back among ourselves. What's the problem?

Because there should be something pretty well defined, because I'm concerned that another paper is going to come out, not published, not in the press, a hot subject finally will come out. We are going way back to the hot zone. It was a rainy day in the L.A. airport, and came up and said, "Here it is." And

"We have found all these new findings." And we're sitting there. And then staff came. And we can't handle that.

Also, as I recall -- John, you might correct me -- I think one criteria I think is important which we have to decide among ourselves, we need to decide do we really mean that this has to be a peer review in a journal before it's brought to the attention or back into this review process or another-look process?

Are we going to really look at something that came in at the tail end of this whole thing as a report, but has not been cleared? Reviewed?

DR. GLANZ: I don't read the review. John reads the review. Why don't we come back to them?

DR. FROINES: I think this is really important. By the way, folks, the number that we adopted for perchloroethylene did not come from a peer-review document. Everybody should be aware of the fact that it came from Del Patterson at MIT in a report that he did. So it was not a peer-review document.

Anyway, I agree with Stan. There are a couple of procedural issues I want to raise about this that relate to formaldehyde. First is I'm a little confused. Jim is reading from Part C. Then you have responses to Part C, but you have also changed the document between these comments and today.

Now, presumably, industry, the public, have had a chance to comment on the revised document, but we haven't seen the

responses to the changes.

DR. ALEXEEFF: No, we received the comments yesterday.

MS. SHIROMA: We did the responses today.

DR. FROINES: Let me just say one thing about that.

DR. ALEXEEFF: It isn't that late. Their comments are in.

DR. FROINES: The thing that I'm concerned about is that we don't get into a situation when we go before the Board, somebody says that the Scientific Review Panel did not have adequate time to review the comments that came in after the revised document was prepared. Because as soon as we get into that, we set ourselves up. Because at the hearing somebody was going through the comments, you and I forget who, and somebody from the Board said, somebody objected and said, "How could you be responding to comments here that have just come in?"

And so there is this problem of perception of has everybody been given an a fair shake if we don't get to those comments until the day of the meeting? And the problem -- and the reason why it's important is formaldehyde, given the level of science associated with formaldehyde, those comments could be quite important.

And especially given the uncertainty around the monkey-versus-rat data. So that's a problem it seems to me.

The second procedural issue is -- relates to formaldehydes is -- the good thing about perchlorethylene --

this is procedural. The thing about formaldehyde that's important, I mean relative to perchloroethylene, is as far as I'm concerned, we have two values. We have Dale's upper value which is the most talked about. Then most of the other values I think we could recognize. We don't really want to pursue them.

With formaldehyde you have a table with a lot of values in it. And I do think that if in the future, the risk managers are going to have to look at tables like that as opposed to just taking the number that we come up with.

Then there has to be -- we have to be very careful to get appropriate discussion of those values in terms of our distributing -- the trouble with our tables is sometimes we have too many risk values and that when you look at it and you say, "Well, how can I make sense out of all this?"

And, you know, on the perchloroethylene there must have been 50 different values.

DR. ALEXEEFF: Over a hundred values.

DR. FROINES: Over a hundred. So with perchloroethylene we were able to focus sort of on two values.

The problem with the table that's so voluminous on values, it's a hard to make a judgment about them. So with formaldehyde in the future, we are going to have to decide how to focus the discussion on a series of specific values and not certain risk assessment.

"You know, you can do risk assessment by about 25

different ways, and let's look at all the values if we do them 25 different ways."

CHAIRMAN PITTS: Let me follow that point. It's a very good point that John raised. I agree completely.

Were these some of the comments on this document? That is, were there comments that we haven't got yet? Substantive comments? I agree completely. I think it's not just perception. It's actually science. It would be hoped that, again, in this process we're talking about in the procedure, we're going to have to see those well in advance of the meeting. That's my feeling.

I don't think it's proper procedure from anybody's perspective to have these, even though we may have in the past. The past is the past.

DR. GLANZ: I recall getting comments before the meeting on lots of things. I heard George say these came in late. When were they supposed to be in?

DR. ALEXEEFF: The original due date was last week some time.

MS. SHIROMA: We did try to accommodate them. They needed a little more time. We were trying to be responsive to that. They needed a little more time. We gave them the rest of the week.

We should go into our presentation. I'm thinking that some of these questions you're asking may be settled with the

the presentation. We are thinking perhaps we should start with Part B since Dr. Froines needs to leave early.

CHAIRMAN PITTS: I was going to start with B for just that reason. There are a number of questions about Part A also, but that's fine with me. Let's go ahead then.

DR. GLANZ: One last thing, do you want to make a motion about the letter?

CHAIRMAN PITTS: I'll do that, too.

DR. GLANZ: Just for the record, since I found people who read these transcripts, I agree with everything that you said, Jim, about the importance of our seeing this stuff, but if something arises, you know, minutes before the meeting, I don't want to establish a precedent that just because somebody gets something here just before the meeting starts that it has to be to taken into account.

Because we are opening ourselves up to being sandbagged. If we give -- people were given the appropriate amount of time to respond, and they come in late, in a way, that's not our problem.

But anyway, I would like to make a motion that we direct the Chair to write a letter to the Air Resources Board acknowledging that in terms of perchloroethylene, there were some procedural difficulties because of the transition to the new streamlined procedure and that we believe it's appropriate to hold an additional workshop. And we'll look forward to the

staff bringing back a revised report to the SRP on that one issue of the best estimate which may end up saying there is no change. Or there may be a change, and then we will act on it or forward it on to the Board.

DR. BECKER: I second.

CHAIRMAN PITS: Any further discussion? Moved and seconded. We will go ahead with Stan's suggestion for a letter. All those in favor, aye?

(There were votes of aye.)

Very good. We will now go ahead, and we will start with Part B on the formaldehyde document.

DR. FROINES: We will begin with the presentation of Part B. George Alexeeff.

(Slide was placed on the screen.)

We have with us Stan Dawson, author of Part B.

DR. ALEXEEFF: With me is Stan Dawson who is the lead for the hard key report, and I will just let him make his presentation.

DR. DAWSON: Good morning. For the record, I'm Stan Dawson, staff toxicologist with the Air Toxicology and Epidemiology Section of the Office of Environmental Health Hazard Assessment. I am principal author of Part B: Cancer Risk Assessment for Airborne Formaldehyde.

In preparing Part B, the staff conducted an extensive evaluation of the published literature with particular attention

to official reviews of cancer assessments by the International Association for the Research on Cancer, IARC, and by the federal Environmental Protection Agency, EPA, and by the Federal Occupational Safety and Health Agency, all in 1987. I have also kept in close contact with EPA's staff and have reviewed their more recent draft risk assessments.

The focus of our report is cancer; however, as stated in the report, formaldehyde is a strong irritant and may be present at irritating levels in ambient air.

I would like to summarize the most relevant findings of our report. OEHHA staff has concluded that formaldehyde, or at least one of its metabolites, can cause genetic damage. Studies in mammals have clearly demonstrated DNA-protein crosslinks due to inhalation of formaldehyde. That's Casanova, et al., 1989, 1991, and even earlier.

Human studies have reported increases in chromosomal aberrations and sister chromatid exchanges in peripheral lymphocytes, but negative human studies have also been reported.

In vitro studies and bacterial studies have produced multiple genotoxic effects. In drosophila, oral administration likewise produced multiple genotoxic effects. And all this has been compiled by IARC.

A recent study by Crosby, et al in 1988 reported a variety of molecular events that underly mutations in E. Coli and human lymphoblasts.

All three of the inhalation bioassays for cancer that have been covered, reported in the literature, showed that formaldehyde produces malignant nasal tumors in rats. Albert, Kerns, and Tobe.

The three largest industrial studies reported elevated rates of lung and upper respiratory cancers. Blair, Stayner, and Atchison studies.

Several studies of professionals reported elevated rates of a brain cancer. Harrington, Walrath, and Stroup.

And a large residential study reported elevated rates of nasopharyngeal cancer. Vaughn.

EPA and IARC in 1987 both determined that there is sufficient evidence of carcinogenicity of formaldehyde in animals and limited evidence in humans. Those agencies therefore classified formaldehyde as a probable carcinogen. OEHHA concurs with this classification.

Also, formaldehyde was identified as a chemical known by the State of California to cause cancer under Proposition 65 on January 1st, 1988.

Of further note is the more recent conclusion by Blair, et al, 1990, in their review of human studies. Quote, it is likely that the excesses of nasopharyngeal cancer observed were caused by exposure to formaldehyde.

OEHHA has conducted a quantitative risk assessment using results from the most definitive of the inhalation studies

reporting nasal cancer in rodents. That's Kerns' 1983 study.

The analysis screened a number of models according to whether or not their predictions fit the data. The models used a tissue-based measure of exposure: DNA-protein crosslinks, occasionally referred to as DPX, From the data of Casanova, et al, in 1989. The multistage result, using GLOBAL86, was a three-stage model.

In response to comments on the first draft of the document, the assessment developed models that explicitly incorporated the effect of cell proliferation. Seven different cell proliferation models, including two-stage models, both one- and two-stage models provided fits of the data.

Because the staff has not previously presented cell proliferation models in the risk assessments, nor has anyone else published work on their use for formaldehyde, I will sketch out our approach now. In the first view graph, the key in the upper left-hand corner -- probably if you could focus that a bit more so the Panel can see it -- shows that, starting on the left, normal cells, Moolgavkar, with a probability of nu zero of producing premalignant.

The premalignant clone then increases with a net rate of K, and the premalignant cells have the probability of nu 1 per cell per unit time of producing a malignant cell. And the proliferation ratio -- really the rate of reproduction of cells at exposure X -- divided by the control rate is allowed to enter

at any or all of the three points indicated at the top of the screen.

The models outside the key represent the mathmatically possible combinations of insertions of the proliferation rate, R. Likelihood procedures then give estimates of the model parameters just like GLOBAL86. The calculations used the same basic bioassay data and exposure data. Most of the models gave a good fit, and several gave only a marginal fit.

The analysis developed scaling factors to extrapolate from the risks for rat nasal cancer to human cancer of the respiratory tract, primarily the lung. Applying the body-surface-area scaling factor of 1.2, which is the default scaling, gave the value of the upper upper confidence limit for the human lifetime risk of, well, q1 starred of 7 x 10 to the minus third.

This estimate used the multistage model which does not explicitly take into account the effect of cell proliferation. Of the models that did explicitly take into account cell proliferation, the five which fit the data well and one which fits marginally gave the increased risk of ten times ten to the of third ppm with a default scaling.

One other model which fit the data only marginally and which appears inconsistent in having a proliferation effect on malignant mutation, but not on the increase of numbers of malignant cells, gave the decreased risk of 1.3 x 10 to the

minus third with default scaling. Uncertainties due to lack of data for the models prevent making a clear choice of models.

In order to take into account the contact mechanism of carcinogenesis for formaldehyde which is a general degree, analysis developed two scaling factors in addition to the default scaling. A generic contact scaling factor purely on allometric or powers-of-body-mass relationships was 5.0. A dosimetrically adjusted contact scaling factor, based on a comparison of the DPX measurements in rats and monkeys was 0.28.

The staff developed this scaling factor in response to comments on the first draft. Available evidence does not permit the establishment of a clear case for either of these scaling factors.

The application of these factors to the results of the various models for respiratory carcinogenesis in rats gave a range of upper confidence level on unit risk of 0.3 x 10 to the minus third.

Each of the individual upper confidence levels on human risk presents the highest value that's unlikely to be exceeded assuming that the particular model provides a practical point of quantitive description description of the cancer process. The range of lifetime risk values represents only the best characterized sources of uncertainty, and there is a big range in that Table 5.

I do point out, though, that the range of extrapolation

from positive animal tests to average human exposure is 80-fold. So this is somewhat less than extrapolation.

The present analysis tested the predictions of the models against the largest human study, Blair et al., 1986. The finding was that the higher portion of the range of risk predicted from the rat nasal cancer was consistent with data on lung cancern from that occupational study.

Now, EPA. EPA in 1987 used a model based on applied exposure because of the apparent unreliability of the DPX data available at that time. That multistage model, using applied exposure requires a minimum of five stages for an adequate fit producing an upper comfort level on unit risk of 16 x 10 to the minus third ppm with no scaling factor.

More recently, a draft update by EPA in 1991 used the new DPX data in a two-stage model, calculating a q1 starred = 2.8 x 10 to the minus third upper confidence level --

DR. FROINES: Could I ask you about that last? You say 2.8 x 10 to the minus three?

MR. DAWSON: Right.

DR. FROINES: Is that based on monkey data or rat data?

MR. DAWSON: That's the rat.

For the extrapolation from the rat there is no scaling factor. And the UCL on unit risk of .33 x 10 using a dosimetric adjustment of the monkey data. Allowing for a 20 percent lower value due to EPA not using any scaling factor, the EPA value

based on the rat data is about half the corresponding value which is considered the best value in the present assessment.

Two highly questionable assumptions by EPA in their quantitative analysis contributed to the lower risk obtained by EPA. The first of these questionable assumptions was to use the chi-squared test for goodness of fit thus allowing the adoption of a poorly fitting two-stage model even though the GLOBAL86 authors advised again using the chi-squared test because of its incorrect rejection rates in just such cases as this one. Use of the Monte Carlo test, as recommended by the GLOBAL86 authors, gives less than a 1.5 percent chance of this two-stage model.

The second questionable assumption by EPA was to use a segmented linear relationship to interpolate between adjacent data points for rat DPX and applied exposure, even though an apparently acceptable mechanistic model to interpolate the noisy data was available and was used in the OEHHA assessment as well as the CIT. In other words, had they just connected up the data points by straight lines.

Furthermore, the EPA update of July 1991 expressed a preference for their risk number based on the monkey data. That's the .33 x 10 to the minus third. But the EPA staff are reconsidering this approach in the wake of criticism received from their Science Advisory Board at the meeting to review the document. And I might add that in the public presentation which I just attended last week in Detroit, the EPA was saying that

they are now planning to use a range of risk from .23 up to 2.8, the first time they are using a range with no best estimate.

The natural occurrence of formaldehyde within normal cells and the steep rise in incidence occurring in the cancer bioassay about 6 ppm both suggest the possibility of carcinogenic thresholds in the risk predictions; however, substantial evidence establishes formaldehyde as being genotoxicessentially implying no defined threshold.

Also, using only the cancer incidence data below the concentration of 6 ppm in a risk model leads to a good fit for a linear model with a risk relationship that has the same unit risk as in the best estimate that we can obtain. So in other words, to weigh the high data point.

The use of the proliferation model shows mathematically and mechanistically how the small slope at low exposures may be consistent with the steep rise above 6 ppm. Thus the OEHHA staff find that the evidence, including the new evidence, against a threshold outweighs the evidence for it.

Based on the finding of carcinogenicity and the results of the risk assessment, the OEHHA staff find that ambient formaldehyde is an air pollutant which may cause or contribute to an increase in serious illness or may pose a present or potential hazard to human health.

CHAIRMAN PITTS: Thanks very much, Mr. Dawson.

Dr. Alexeeff?

DR. ALEXEEFF: Yes. We received two sets of comments. One was from the EPA, and that was specifically solicited by Dr. Dawson. He asked EPA to comment on our document since this seems to be a very controversial issue. So Stan will summarize the EPA comments and respond to them.

DR. GLANZ: Are they very long?

DR. ALEXEEFF: You want the whole letter?

DR. GLANZ: Since staff was such a -- that was a big issue in Part C.

DR. DAWSON: We received the document with the proposed identification of formaldehyde but not until October 7th, 1991 although the cover letter was dated September 20. Thus there has not been sufficient time to review the document thoroughly especially the new sections on cell proliferation models.

In an attempt to meet your October 15th deadline for the comments, we have a preliminary list of remarks. The summary is on pages 1 through 3 and 1 through 6 and should indicate more thoroughly which UCL will be incorporated in cell proliferation.

The discussion concerning scaling factors is not quite clear as to which unit risk estimates incorporate which scaling factors. My understanding from Appendix A is that cell proliferation modeling was ultimately not done and the default scaling at 1.2, which is considered the most interpretive. These sections should incorporate better -- do you want me to read just straight through?

The best estimate of UCL, which is on Page 1 - 6, would be better described as your most plausible evidence because the best estimate has become statistical jargon which implies a different situation than is described. Incidentally, this value of 7 x 10 to the third ppm most of the value of the ppm is considered an upward value for its range of UCL values. EPA will not use a single unit risk.

Relationship of predictions to observe single unit risk, Page 2 - 20. The use of lung cancer incidence and the assumptions of two parts per million associated with nonsedentary activity are not adequately justified. In relation to formaldehyde exposure, lung cancer was not as clearly in excess as was nasopharyngeal, the Blair et al study.

Concerns were noted in the document explaining why the excess lung cancer may not be entirely free from formaldehyde exposure. In addition, it would probably be more militant to have the exposures in less active scenarios in trying to generalize the situation.

And the next point, page 2 - 10, the first sentence. The estimation that was used for the dosimetric model involved in the procedures to obtain an estimate for the binding of formaldehyde to DNA, (1), the exposure to concentration X, instead of obtaining, which would probably be a straight line.

The discussion of the third scaling factor, the final premise, the discussion of the third might be easier to follow

on page 8 - 14.

And the closing paragraph: A more complete list of remarks on this document will follow in a few days from the Health Environment Review Division.

DR. ALEXEEFF: They have told us they were not going to send any more comments.

I now will just very quickly go through and pick up some responses to those points. Okay. Well, the first point is about the clarity of the discussion in the summary relative to what's in the text, and I think it would have been all cleared up if they had found Table 5. All I can say is I will try to go back and make that clear.

And the next one is EPA desires to use the most plausible value instead of best estimate for like our 6 x 10 to the minus third. To me, that's kind of a -- we have been calling it best estimate for a while now. To change that over it would take, I guess, a policy change.

DR. ALEXEEFF: We have tried to be flexible on the terminology in the sense that we did not want it to be a statistical term, so we could change it to "most plausible value" if you thought that was better. We could go through that summary and change the words "best estimate" to "most plausible value."

DR. GLANZ: I think "best estimate" is okay.

DR. BYRUS: Is "best estimate" a statistical term? Is

that official to use that?

DR. GLANZ: Well, yes and no. And you get into the question of what "best" means, and there are lots of different best estimates.

DR. FROINES: I don't agree at all. The issue around perchloroethylene just used "most probable upper bound" and what was the five percent level that Dale used; do you remember? It was an average value or best estimate.

DR. ALEXEEFF: I forget his terminology.

DR. FROINES: But these terms convey meaning and, frankly, I don't know what we mean by "best estimate" in this case. In this case I must admit I'm confused about what, quote, is the best estimate. I don't feel really comfortable with any of them in a certain sense as to what best estimate. I don't know what "best" means. Does it mean -- I don't know what it means. I think we have to be very careful about the way we use these terms.

DR. GLANZ: Well, I think that's a different argument. I think that when we say "best estimate," we are using "best" in the sense that normal human beings use the word "best," and that is it's the one we think is the most reliable and more standard than any others.

In statistical terms when you talk about "best estimates" that has a specific technical meaning in certain contexts. But What "best" means is the best. And squares estimate, there's a

whole variety of best estimates. So I think the specific point that EPA was raising there, I don't find a problem.

Now, if we don't want to use the word "best" because it would be in the way a normal human being would use "best," that's a different issue.

DR. FROINES: It's very, very policy-driven, because in perchloroethylene we said our best estimate is in fact the most probable upwardbound, so everybody at this table should understand it. They accepted the most probable upwardbound as their best estimate.

I don't know if that's the best estimate, and I don't want that the particular sentence to be taken out of context, but the point is it is driven by the fact that George used an upwardbound as a best estimate.

DR. GLANZ: Well, that's right. But what I'm saying is that's a different point than what the EPA is raising. They're saying that we're using that as a specific statistical technical term, and that should be avoided for that reason. And I don't agree with that.

DR. ALEXEEFF: We have always had difficulty in deciding what to call it. After what Dr. Froines said, it makes me think that maybe a good term might be "best upper bound value." We would be happy to go through and change that term throughout all the things because that's what we are talking about. We present a range of upper bound values, and we are saying that within

that range of upper bound values, this is the best upper bound value.

DR. FROINES: I think it would be useful for you to prepare a series of definitions that say, "These are the terms we are going to use, and this is what they mean." And I think we could adapt to whatever they are. And we should know what your definitions are. It forms the basis for our conclusion.

CHAIRMAN PITTS: I think there should be a glossary of terms or something in the documents.

DR. FROINES: In the appendix. I quite frankly am confused.

DR. BECKER: I'm going to make a comment just in general on this particular document, and that is the overall complexity of this document is far greater than anything which has preceded it. Now we have gone to DNA binding, and we are getting complicated factors such as cell proliferation, so this is by far the most complex, the most technically challenging. And yet the executive summary doesn't, at least from my perspective, especially that table, it needs definitional things that we can agree to and come back to trying to read this in terms of in light of the other things.

This has gone to the next generation. We have gone another step further. So we need definitions, and we need some firm basis on which to say, "We accepted this based upon this." Does that make sense? The other people on the Panel may not

have felt that way.

CHAIRMAN PITTS: It makes a lot of sense.

DR. BECKER: Could I ask you one quick thing? The table in the executive summary, that gives an incredible number of indoor air quality as opposed to outdoor air. That person might say, "Well, holy smoke! You have got -- I forget how many -- five or six thousand exceptions in the outdoor represents a relatively small thing, so it's almost a statistical argument.

You could say, "Wait a second. Is that really meaningful?" What I was getting at is we need definitions to put some of these in perspective at least from my perspective.

Do you, in response to that, when you're dealing with formaldehyde as a toxic air contaminant, are we considering the indoor environment in the light of cigarette smoke? That's all part of the course.

CHAIRMAN PITTS: That's a very deep question. I would like to follow up on what Chuck has said. Does the ARB, then, have the regulatory authority to regulate the sources of indoor pollution?

MS. SHIROMA: We do not at this time. But the CAT statutes specify that we are to discuss indoor air, because the data are available for indoor air.

DR. BECKER: I understand that. You can understand my feelings. You have got such an overpowering driving factor. We're really talking about -- we have to make that very clear.

That's why I like that table in the executive summary, but I wasn't sure of all the wording. If you could make that clear.

MS. SHIROMA: Perhaps one other piece of information we could add to this discussion. If one would be exposed to the outdoor levels for the 70-year lifetime, what would that be? In that case you could compare formaldehyde against the perchloroethylene.

DR. BECKER: That was one of my comments. The thing that makes this compound difficult for me was the level of the scaling factor is complicated. New findings, models were added and -- but then that comparison. Because fundamentally we have the toxic air contaminants. We ought to be able to erase that from the outdoor.

DR. ALEXEEFF: Well, that's that table you found. I think it does that rather well. Even from the outdoor perspective, it's a greater impact than most of the chemicals that we looked at.

DR. BECKER: That's exactly what I thought. My perspective was that, yes that it these are pretty nice tables. Where you put the unit of the risk for the outdoor even by comparison with that. Do you understand? In other words, that number still has merit.

MS. SHIROMA: I think right now it's contained in your draft finding, the comparison of the unit risk. But I understand what you're saying. You need to have some reference

to the outdoor.

CHAIRMAN PITTS: One last point. I think this is an issue now that has been of great concern. If this is released, and it says 7,000 cancer deaths due to the indoors, and there has been a great deal of response from industry and from the public. I'd like to ask the question: What agency is responsible for controlling indoor air pollution?

Because this broad -- everything we have said so far, this number is greater than the sum of all the others I will bet you, death by cancer, by everything else we have looked at, this one number. And it seems extremely important that the Air Resources Board have a statement as to this is the number, and this is how it comes out, and this is how one expects to proceed in terms of treating this situation.

And I don't know. I don't have an answer to that, but I hope somebody has an answer to it. Because that's the big question. That's the 7,000 question.

MS. SHIROMA: And I'm not sure that we can simply address what that next step would be in terms of taking that data, because the response rests elsewhere at this point in the state agency.

CHAIRMAN PITTS: I understand it's mismanagement, but I sure hope it's communicated from the viewpoint of communication. I hope that the -- I presume they are well aware of this.

DR. GLANZ: We can add a statement to that effect in the

findings.

CHAIRMAN PITTS: I think it's a -- I would hate to see us proceeding from the Panel's point of view. I would have to make it very clear that we recognize just exactly what Chuck has seen, and what we have seen here, and that the -- we can worry about this later, expresses its interest and concern and interest in the fact as to how this will be treated in terms of whatever risk management. That's a risk-management decision. That's somebody else's decision, but we have a great interest in it.

DR. ALEXEEFF: I think Stan still has a couple of --

DR. DAWSON: I will go very quickly through. The next one was the question about the observed to predicted values, and the EPA was being critical of our use of basically doubling the actual exposure to account for the fact that the workers were ventilating approximately on the average twice what a sedentary adult would be ventilating. And I guess my response to that is, you know, we can -- in particular, they didn't think it was documented sufficiently, and the number came from our Occupational Health Program and the standard value that they use

And I can certainly go back and double-check the sources on that and the data and see about that.

DR. FROINES: Why do we need to do it that way? Why can't we say it like it is? If we say that their intake is so and so because they are --

DR. ALEXEEFF: Exercising? Moving around? Physical labor?

DR. FROINES: Adjusting the actual exposure level.

DR. ALEXEEFF: Well, It's so much easier mathematically to do it this way for one thing, and it seems to me to be conceptually good.

DR. DAWSON: All we did was increase the ventilation rate, use a standard occupational ventilation rate instead of the standard sedentary information. That's why the exposure is greater. We don't see this as a controversial issue. We always assume that people involved in occupational environments are breathing more heavily than we are sitting here, and the standard assumption is twice.

DR. FROINES: You are talking about doubling the concentration I thought you said.

MR. DAWSON: Yes. Yes. Well, what goes into there is a rather complicated formula, the dosimetry of it as well. Well, basically, the idea is simply the rats are at rest, so you ought to compare it, first of all, to resting humans and take into account the fact they are really getting twice as much formaldehyde.

The next point was kind of a technical point about least breath procedure, whether or not you were fitting versus the exposure concentration or whether you were fitting between predictions of absorbed -- I'm frankly somewhat at a loss as to

why they are worried about that. I will check with them. It's basically quarreling with the word as far as I'm concerned.

Okay. And they want dimensional units on the variables on the table -- that were included in the scaling factor and that certainly --

CHAIRMAN PITTS: Is that basically it?

DR. ALEXEEFF: There are still other comments on the formaldehyde. There were six actual comments. They were very similar to the previous comments we received, but I was wondering if it made sense to go through Table 5 just a little bit to sort of clarify this -- the different risk assessment approaches that we used.

CHAIRMAN PITTS: What page is that?

DR. ALEXEEFF: Page 2-24.

DR. FROINES: But George, are the formaldehyde comments germane to this?

DR. ALEXEEFF: I can go through these comments. It refers to these kind of numbers. I wasn't sure how comfortable you felt, based on Dr. Becker's comment about the large number of numbers. If you want to go through that -- or should I go through the comments? That way I think you will clearly understand the depth of their question better in terms of comparing the various numbers.

DR. GLANZ: I'd like to go through Table 5.

DR. FROINES: I, by the way, don't think it's the crux of

the question.

DR. ALEXEEFF: Oh, you don't?

DR. FROINES: No. Because I think we now have .3, three-tenths to the minus three from EPA that does not appear in Table 5. So we do have a problem.

EPA's latest 1991 document using monthly data has a .3 value and -- oh, pardon me. Okay. You do have a .3, but I don't think it's the same.

DR. DAWSON: No, it's not the same, but the idea of -- I think that I systematically did not put the EPA rat material in because it is more problematical. They used to stamp this stuff "Do not cite in the quote."

DR. FROINES: We have been through that before. We agreed with methylene chloride that we wouldn't take into account those values as they exist, and we could not take scientific values into account just because they're draft comments.

DR. ALEXEEFF: And with methylene chloride, we were dealing with a 1987 draft, and we had a 1989 report, something of that nature. So we had a couple of years over the EPA report.

In this case, EPA is developing it concurrently with us. We're sending out a draft, and they send out a draft. And generally speaking, the draft is 1991, November. So that's just a couple of months ago. So there would be no way we could have

their estimate in this draft, you know, because of our preparation of that.

DR. FROINES: I don't want to stop you from Table 5, but I do want to point out that you and I are going to be before that Air Resources Board in a few months to present formaldehyde, and I guarantee that the monkey data from the EPA assessment is going to appear before us raised by somebody else or by us. And I think we have to address it.

DR. BYRUS: I would like to discuss the use of the monkey data that arrived at that number. I think the document is pretty well-written, and I could understand anybody -- I have trouble with it. I just would like to hear what EPA's rationale was.

DR. ALEXEEFF: Dr. Dawson can correct me, but the EPA monkey data is essentially the star data for all intents and purposes, essentially the same number. So as I think I go through it, which would be a 54-fold adjustment. In other words, a 54-fold lowering of the concentration by using the monkey data.

In our analysis of the monkey data, we suggest a 18-fold adjustment. Now the reason for that is --

DR. WITSCHI: What exactly are the monkey data?

DR. ALEXEEFF: There were studies conducted where they dosed animals to radio-labeled formaldehyde. Rats and monkeys. These were acute studies, right?

DR. DAWSON: Yes.

DR. ALEXEEFF: And they compared the binding of formaldehyde in the respiratory tract between the two species. Now the advantage of rat binding is concentrated to a very small portion of the nasal area. They are obviously nose-breathers, and because whatever the geometric nature of their noses ends up having most of the formaldehyde binding in a very small location.

For the monkey, which breathes through both nose and mouth as do humans, the binding for a large part for the highest concentrations is also in the nasal area. But there are also bindings throughout the whole respiratory tract, because our nasal passages are not as small as the rat. So more gets through.

So the issue of the comparison is depending upon how data was prepared by the CIAC for binding at a couple of locations in the rat and in the monkey, and there were a couple of different dose levels. So depending on which dose level you choose and which region you compare --

DR. WITSCHI: Meaning concentration?

DR. ALEXEEFF: Concentration of the formaldehyde. Depending upon the exact comparison you make, you can get a slightly different number depending upon the region of the nasal area here, comparing, and the dose level.

DR. WITSCHI: The monkeys got more data?

DR. ALEXEEFF: Yes, the rats were completely concentrated in that nasal area, and the monkeys were throughout their tract. And this is consistent with other cell-proliferation data in the monkey which shows cell proliferation throughout the respiratory tract.

DR. BYRUS: The data, wasn't it bound formaldehyde? Not formaldehyde --

DR. ALEXEEFF: This is bound formaldehyde. DNA formaldehyde. We are getting down to the crux. This is much more refined than anything we have looked at before. This is not just tissue concentration or something like this. DNA-bound formaldehyde.

DR. WITSCHI: C-14.

DR. ALEXEEFF: Yes. C-14, right.

DR. WITSCHI: Not exactly formaldehyde anymore.

DR. ALEXEEFF: So in some sense this is a much more extensive analysis, and the problem that we had with using this data -- we have done the calculations with this data. Well, first of all in our 18-fold adjustment, when we use the monkey data, it's 18-fold because we try to use as much of the monkey region as we can. We would like to use all of the monkey, because of the sensitivity of measuring formaldehyde, they can't -- it sort of disappears as it gets to the larger and larger volume.

DR. WITSCHI: Can I interrupt you. I thought by using

the monkey data, the unit risk becomes smaller.

DR. ALEXEEFF: Right. The unit risk becomes smaller --

DR. WITSCHI: One more interruption. The comparison?

DR. ALEXEEFF: The comparison is based upon the highest concentrated point between the two species; not the total bound between the two species. They didn't have data from the total bound in the respiratory tract which is what we think would be necessary to do a monkey-rat comparison. Ideally you would want to know the total bound in the monkey respiratory tract and the total bound in the rat respiratory tract. And then that would be your comparison.

Then what we can do is we can compare the total bound in a very small area of the rat and the total bound in a very small area of the monkey. And that's the comparison.

DR. BYRUS: So that's the comparison? They didn't adjust it at all?

DR. ALEXEEFF: They couldn't. Because for any particular region of monkey nasal tissue, the concentration of bound formaldehyde is less. Any region. And that's the comparison, the concentration of bound per region.

DR. BYRUS: I'm really confused now. Like per area?

DR. DAWSON: Basically per area. It's an effect that was really per gram of tissue, and they had obviously excised the tissue.

DR. BECKER: Maybe I'm naive about this. This was the

other complexity I was talking about before. This level of complexity is a nice idea, but has it been related clearly to the level --

DR. DAWSON: That is one of the issues, the level of complexity. This document brings in the level of complexity.

DR. FROINES: Can I just follow-up on what Chuck is saying? Because I think it's an important issue. And that is one of the things that comes up all the time, comes up from its own proliferation, and it comes up with the kidney tumors, and the proteins, and it comes up here with markers.

I'm very interested in markers, so it does seem to me that it would be worth trying to think about what information pretty much falls into the category of research as a research issue that still needs to be developed, and what is information that is sufficiently developed that falls into a category that would be appropriate for regulatory purpose. And clearly those are going to overlap.

But it does seem to me -- I think that's what Chuck's getting at. In some cases there is still sufficient uncertainty about the research issues that we have to be careful about bringing them into a process which is in essence an ultimately regulatory one.

DR. ALEXEEFF: Well, that is why we present the monkey data included in the range, but it's not our best upper bound value. Instead, though, I think there is a very good argument,

a very good understanding that the area where the radial label has bound in the nasal epithelium is also the area of tumor development.

The area of the rat nasal epithelium to which the C14 is bound I think is fairly well correlated with the site of tumor production in the rat. So that's what we are calling our tissue-dose model or what's referred to as DPX. That's the jargon that EPA created.

So we -- in the original EPA number in 1987, they just used our old-fashioned style of exposure concentration and came up with a risk number. That's what this top row on Table 5 is applied to is this model. And that first one, the 15, is the current EPA value, the one that's been approved based on the '87 draft when we first started this process.

Then the next thing, the tissue-dose model, the next line, refers to this DPX. So this is binding. This is incorporating the data of the C14 binding in the rat epithelium. And we feel fairly confident about using this data.

Although it is very close to the frontiers of research, we don't feel justified to ignore this data, this risk estimate, and it does lower the potency. That's why we would lower our risk number from 15 to 7.

So if you went to the current, applied this information to this findings on DNA, it lowers the risk estimate, and we feel very confident.

DR. WITSCHI: Those came about by not comparing monkeys, but comparing the rats and the mice.

DR. ALEXEEFF: Right.

DR. WITSCHI: The mice have fewer tumors and with it was found out that they have less tissue dose.

DR. ALEXEEFF: Right.

DR. WITSCHI: The monkeys have a totally different life span.

DR. ALEXEEFF: Right. You're correct. So that is the tissue-dose model.

Now the next set of values is the cell-proliferation thing that Stan worked on. So let me just ignore the cell proliferation at this point and go across the columns. And that is okay.

The first scaling type is none. What that means is this is -- we generally have in our guidelines, it suggests that we should scale from rodents to humans based on surface area conversion. We have discussed that many times that surface area conversion is, unless there is other clear information, it should not be done. That's what we use. That's our policy.

EPA did not do that for formaldehyde, although they did do it for methylene chloride. It's really not that clearly justified as far as we can tell, but that was their choice. So the "None" refers to the scaling.

In the next column, systemic default, that's the systemic

default scaling. And in this case for formaldehyde. It's an increase in the potency by 1.2, about 20 percent. So it's not a dramatic change.

Now the next column is some other work that we have been looking at in the Department, in the Office of Environmental Health Hazard Assessment. In trying to do comparisons -- this is since we are assuming that formaldehyde is causing carcinogens in the respiratory tract, and it's not a systemic.

Therefore, we're thinking instead -- the default scaling is really based upon systemic arguments. So we try to evaluate simply lung-comparison arguments under that part of the analysis here. So from that circumstance, it would be a five-fold increase if you were comparing the number of epithelial cells in the respiratory tracts between the species.

But this is still very preliminary in our sense, so we just presented it as, you know, a scaling approach that has been discussed previously in the guidelines, but it's not our generally accepted approach.

DR. WITSCHI: You know, George, what you are talking about, if I understand you correctly, these are trivial changes in the unit risk or in this table compared to the one -- if I'm correct -- which is about the factor of 50 if you include the monkey data. Now, that's a big change. All the other ones here, scaling or not scaling, is most trivial.

DR. ALEXEEFF: That's the last column of the monkey data.

Contacts asymetric with the monkey data. So what this is doing is saying, "Okay. We know you have got the risk-estimate data from binding to the nasal epithelium of the rat, but the nasal epithelium of the monkey doesn't bind as much. Therefore, you should reduce the potency by the factors that they bind."

DR. BYRUS: Based upon the fact that you're deciding to adopt the tissue-binding data, then that argument does make some sense.

DR. ALEXEEFF: So we present that argument, and we would, based upon the data that is available, we would compare a slightly different portion of the respiratory tract in the monkey versus the rat.

DR. BYRUS: Could you run through that? You didn't quite get to the end of that. I didn't quite get the crux of why you -- I understand that the experiment was done. I didn't see the original data, so they looked at the bound formaldehyde on the DNA, but they are only taking individual samples, and they did not do a total bind in that, they didn't get the total amount of a formaldehyde bind. You compare the total amount bound in all the DNA in the respiratory tract, the rat versus the monkey. You did not do that, right?

DR. ALEXEEFF: Correct.

DR. BYRUS: You are saying that that would really be the accurate the comparison for extrapolating --

DR. ALEXEEFF: Right.

DR. BYRUS: -- the total amount bound, then theoretically would be the same dose.

DR. ALEXEEFF: Right.

DR. BYRUS: They did not do that. They just took individual tissue sites, and since the rat is more concentrated anatomically, it has a much higher binding.

DR. ALEXEEFF: Correct.

DR. BYRUS: Am I right?

DR. ALEXEEFF: You're right.

DR. BYRUS: Well, that makes sense. For that reason I could see not taking that data, extrapolating the monkey data.

DR. FROINES: This is all acute data. We have a problem with using acute data.

DR. ALEXEEFF: Acute data is a very good point, because that is the answer to the cell proliferation information that I will present next. If we feel squared on that, I'd be happy just to tell you what happened with the cell proliferation data.

DR. FROINES: It is important to be clear that in the human epidemiological data, there does appear to be a dose effect. It's not just an animal issue whether dose rate effect is relevant.

DR. DAWSON: Yes, but the dose rate effect would be taken into account in part by use of these data in animals. At least that gives you what looks like a dose rate effect, but it's really DPX effects.

DR. BYRUS: I think the other concern about the monkey data -- tell me if I'm wrong -- the monkey might repair this factor faster than implicit in the interpretation of that data? Or can't you make that interpretation?

DR. ALEXEEFF: That was a comment we made in response to them, and we are trying to understand why the concentrations might be so different in that area. And that is more than one possibility. We don't know a lot about the monkey like we do about the rat.

DR. WITSCHI: Well, you certainly don't know if a monkey is cancer proof.

DR. DAWSON: No, we don't know.

DR. ALEXEEFF: Now, what happened in the cell proliferation, and I think that -- we only take cell proliferation into account.

This is -- as far as I'm concerned, this is on the edge of the frontier of research. I think it's important to try to go as far as we can. And it was really Dr. Froines' suggestion that we include cell proliferation data.

Now, originally when cell proliferation studies came out in '83 by Swenberg and in '88 by Zwart, et al., they are based on acute studies. What they did is they found that the cell proliferation in the rat was increased dramatically at these same concentrations that the rat bioassay was done, a very high rate of cell proliferation, and that they were saying that this

cell proliferation essentially results in the tumor genesis and not, you know, toxicity.

So what has happened in 1990, the CIAC, the Monticello and Morgan, they finally completed six-months and 12-months cell proliferation studies in the same rat. And what happened there is that proliferation is an acute effect at the lower dose level. It's not a chronic cell proliferation. And there was also a 13-week data point which showed that the cell proliferation rate was already increased dramatically.

So at the dose level, the dose level of of six parts per million which was one of the bioassay levels of the elevation in tumors, the cell proliferation rate in the rat nasal actually -- you know, the numbers reported actually fell below the background level for controls. So I mean that's just an issue of noise.

DR. BYRUS: A longer term. What month --

DR. ALEXEEFF: Six to 12 months. They had six months and 12 months.

DR. BECKER: Doesn't that call into question the whole --

DR. DAWSON: At higher concentrations you did get the ten-fold.

DR. ALEXEEFF: Still at the highest one, you still get the highest cell proliferation. And so cell proliferation is not -- instead of it being a very similar type of a response, it shows elevation at all the dose levels. In the chronic, it was

only at the highest dose levels that the proliferation was so high.

DR. BECKER: 13.7 parts per million?

DR. DAWSON: Approximately.

DR. BYRUS: So acute occurred even at what low dose?

DR. ALEXEEFF: I think it was all the way down to one part per million.

DR. FROINES: The data are consistent with the theory such as if you deal with cell proliferation, the level is going to go up at the low-dose range. So what you found is what you would expect to find: that when you take into account cell proliferation, your risk will of necessity go up.

DR. ALEXEEFF: The risk will go up. It depends on what is driving the risk at the lower bioassay doses. If, for example, the cell proliferation rate as in the chronic syndrome was the same as the acute symptom, then probably we would have found a lower potency, and that's why in the comments, Starr's original comments in here, he says he expects a maximum 20-fold increase in net if we use cell proliferation. The actual study showed ten to 20 based on the dose level. So that says something about acute data.

The chronic data --

DR. FROINES: Let me ask you one question, because I'm not sure it's worded correctly. On Page 2-6 you say.

(Reading)

Although the relationship between cell proliferation and tumor response is uncertain, the increase in the rate of cell proliferation would increase the opportunity for formaldehyde to interact with DNA in turn increasing the likelihood of formaldehyde-induced mutation and formaldehyde-initiated cells.

(End of reading)

Are you sure that's what you want to say? Because in part what's really happening is -- what you're talking about is cell proliferation enhances the fixation of the cells to facilitate initiation, and it's not simply a question of increasing -- it would increase the opportunity for formaldehyde to interact with DNA.

The important thing is you have got formaldehyde bound to DNA. You're killing cells, and so you get hyperplasia as a response, and those DNA adducts then result in mutations because of the fixing of the lesion in the DNA. So it's a little different from what you have said here.

DR. ALEXEEFF: That's true. Except in this case it's kind of a combination. I think your point is correct as well. I think it should be both things.

In this case we actually have the binding data with the DNA, so we also can make the statement that there is an increase in binding based upon these acute studies, where in normal

cases, we are simply just assuming a cell proliferation period. Because we don't know about the binding of DNA.

So it's a little bit -- I think you're right, and I think this is right. But I think the actual right answer probably is a little more of a combination of the two.

DR. FROINES: Yes, but he says earlier -- I think the point that you're making -- he says, "Thus a ten-fold increase in dose yields a greater than ten-fold increase in binding."

DR. ALEXEEFF: That's what was reported, yes.

DR. FROINES: So that goes to the issue. All I'm saying is you say that same thing twice without addressing the other aspects of the cell proliferation.

DR. ALEXEEFF: Okay. I see your point.

DR. BYRUS: Let me ask one more question about proliferation so that I'm clear. Are people arguing, then, about the -- if something increases the rate of cancer by proliferation say independent of it being binding to DNA. Say something that doesn't react to DNA, doesn't increase proliferation.

The argument, then, is that usually only occurs at higher doses, so I can't extrapolate down to the low-dose effect, because there is no low-dose effect. All right. Now, are they saying -- in this case here you have something that obviously does bind to DNA and obviously something that does cause proliferation. So it's mainly the lack of extrapolation.

Because if the proliferation effect, if there was a long-term proliferation effect as well as the acute effect, people would be arguing that really there would be less risk because this effect would only occur in high doses; is that right?

DR. ALEXEEFF: Yes.

DR. BYRUS: Independent of whether or not -- but we're saying because it binds the DNA, it's going to bind the DNA in all doses. And it may be more likely if cells are proliferating, but it's going to bind anyway.

DR. ALEXEEFF: And we have seen binding at levels below the proliferation level.

DR. BYRUS: That's right. That was my contention. So it is clear that binding, they measured binding when they went to this more sensitive assay.

DR. ALEXEEFF: Right.

DR. BYRUS: At doses that occur below the proliferation level; is that right?

DR. ALEXEEFF: Binding has been measured at the lowest dose tested, .3 parts per million in the rat and .7 parts per million in the monkey.

DR. BYRUS: At .7?

DR. ALEXEEFF: Yes. And those are both for levels of even acute proliferation.

DR. BYRUS: Even acute proliferation?

DR. ALEXEEFF: Apparently in the chronic and in the acute, one part per million.

DR. WITSCHI: You can't really say, because the order of man will be more sensitive than the averages we have for monkeys.

DR. FROINES: Good point. There's no question that you can get DNA binding without having cell proliferation certainly.

DR. WITSCHI: Well, we don't know. What I mean to say is the access to cell proliferation, they are not very sensitive.

DR. FROINES: So I have to say based upon the existing data, this what we're detecting, that the binding is several levels below the level of cell proliferation is being detected. And the detection limit is based upon the sensitivity.

CHAIRMAN PITTS: Could a simple old physical chemist ask a question here? As I recall, in the big workshop in the discussions one of the points was that -- to put it in the simplest terms I can think of, is the problem with extrapolating from high, probably high, ten ppm formaldehyde, carcinogenistic potential, if I can use that term, extrapolating down to where you would be at 1 ppm or half a ppm, when you got above the certain level of formaldehyde you're actually prohibiting or interfering with wonderful mucociliary clearance, and your're actually -- the mucous layers can trap formaldehyde at levels of -- again, the mucous layers can trap formaldehyde thus preventing it from reaching the underlying epithelial layer is

the idea that you have too high a concentration. You knock out the epithelial layer. That is the idea? You knock that out?

DR. ALEXEEFF: Well, that is the argument that is being suggested.

CHAIRMAN PITTS: That's it.

DR. ALEXEEFF: But we found 90 below was one part per million. That is the cutoff, and that's I mean by them.

CHAIRMAN PITTS: So that shoots the argument down presented in the workshop. You can't extrapolate because you're screwing up the epithelial layer by these very high concentrations. Is that what you're saying.

DR. ALEXEEFF: I would question it.

CHAIRMAN PITTS: Well, you can't respond with another question, however.

Could you not also -- there is an indication that perhaps there would be a problem at lower levels of formaldehyde if you breathe real air. Real ambient air has ozone in it, has formaldehyde in it. These studies, as far as I know, are done in clean air.

DR. ALEXEEFF: Right.

CHAIRMAN PITTS: Well, I don't think that's what you're breathing when you breathe formaldehyde. Even formaldehyde indoors is when you have got a gas stove on for example. That's it.

DR. ALEXEEFF: As Stan pointed out --

CHAIRMAN PITTS: You might want to add that, by the way, somewhere, regarding clean air. Because I can go back 20 years, and they are talking about an ozone standard for pure air. Finally they are coming around to remember that there really was oxident, and you do have a multiple impact on multiple species on your system. Just a footnote I think. Footnotes are okay.

DR. ALEXEEFF: One thing I wanted to say is that this extrapolation, though, that we're doing amounts to high levels of only eight-fold, whereas for perc it was a hundred thousand. In terms of -- we are arguing these issues like the mucociliary layers, DPX, but the extrapolation is not as great as what we have been dealing with. And we have got so much data showing things are happening.

DR. BYRUS: Is that reflected in the executive summary? The statement you made, it would seem to me to be something useful to have in the findings, the summary, just a comment because we have the table, and we hear all this about extrapolation. And it's kind of nice to see somewhere the point you just made which seems pretty relevant.

DR. FROINES: I just had one procedural issue I would like to raise. It's 11:20. Two of us walk out at 12:00. I think that brings us below a quorum if I'm correct. Should we go ahead with the discussion, continue the discussion as it's going, and just take up the rest of this compound the next time we meet? How do you want to proceed?

CHAIRMAN PITTS: Genevieve, what's your comment?

DR. FROINES: There is one reason why I asked that question. While I was listening, I was also thumbing through the Formaldehyde Institute comments, and they clearly make significant comments about the epidemiology. I have some problems with the way the epidemiology section is written, because I don't think it includes some of the data that is below the standard. But I think it's relevant.

And, thirdly, I think it's unfortunate that Dr. Friedman isn't here, because he's our epidemiologist, and obviously this is a very complicated epidemiologic issue. So if we did carry it over to next time, then maybe Friedman could be here to comment on the various aspects of the epidemiology.

MS. SHIROMA: Well, given that you will lose your quorum, you would be unable to make decision today. We do have a meeting scheduled for December 5th, and we're just getting ready to mail out the report. So an option is to continue the discussion at the December 15th meeting.

DR. FROINES: If we do do that, can we then get detailed responses to the comments that are coming in? For example, the new EPA numbers seem to me to need to be addressed. The points in the formaldehyde documents need to be addressed.

DR. DAWSON: I think the formaldehyde documents -- I think I would know how to address them, and I assume that --

DR. ALEXEEFF: I'm prepared to respond to them today if

we have time, but I think it's more important to go through what is the substance of this chemical, and why we have all these numbers. And if we wanted to defer that until you have had a chance to review it, there are comments --

DR. GLANZ: Could I just ask a procedural question. I am relieved that we are not going to be forced to make a decision on this by noon. In light of the discussion that we have had today and these new comments from the Formaldehyde Institute, if any changes get made to the documents, do we then have to go back out to public comment?

DR. ALEXEEFF: We don't expect any changes from formaldehyde. We don't expect any changes. We did have a couple of changes that Stan mentioned with regard to the EPA comments, a couple of pointers to the table to clarify what we are talking about and we can put in the glossary. I don't think that requires -- I think those can be almost just as the final editing changes that often occur in the process.

DR. GLANZ: So we wouldn't get another draft of this between.

MS. SHIROMA: No. The same applies to the public hearing.

DR. WITSCHI: If I might bring up something which is in Paragraph 10 on the draft report of our finding which is -- would you say there is a result to exposure in an indoor environment? And I haven't found anything of this being said in

the document.

DR. ALEXEEFF: I think on the actual findings portion of it that's actually -- those are things that you as a Panel can conclude or not conclude, and you can strike and revise the findings of the final meeting. The findings are separate from this. That's starting information for you to go to to any conclusion you want.

DR. WITSCHI: Am I correct, this is not being discussed in the document?

CHAIRMAN PITTS: To clarify it, these are effects other than cancer. And I have a big sign on that too. I than haven't seen those findings. I have seen them, but I haven't gone through them.

MS. SHIROMA: I just want to clarify that draft finding that you're referring to, Dr. Witschi, is from the risk assessment discussion executive summary where the Health Program will determine what the outdoor computations would be as compared to the indoor computations.

DR. WITSCHI: Well, yes, I found it in the executive summary. But that executive summary wouldn't affect the document. You have got to have something in the executive summary that's not in the document.

MS. SHIROMA: Well, what we do in the executive summary is meld the Part A computations with the Part B, Health. The only other thing is the risk-assessment discussion.

DR. WITSCHI: But there are things in the executive summary that I didn't find in Part B.

DR. GLANZ: Again, point of order. Since we have sort of decided that this is going to be continued, and since we are sort of getting Table 5 explained to us, I would request that we go back to what George was talking about before. And we can deal with the findings later, because this is a very complicated document.

Although I think in many ways it's doing a lot of the things that we have tried to do or talked about before. It's just getting down to molecular mechanisms.

I would like to say in addition, why are we doing this?

CHAIRMAN PITTS: Postponing a decision to the December 5th meeting, it seems to me we will be making this decision not necessarily entirely on the fact that two people are leaving, and there is not a quorum, but I would suggest that it's a very complex issue, and as a matter of fact, we would be following the suggestion of the Air Resources Board to act carefully. And carefully take the time to examine it well from all sides even though we may say, "Well, we won't do much."

And that falls in the spirit of what Jack suggests, that we are very sensitive and proceed on that basis. And it's important that all areas get explored carefully and numbers come out careful.

And would you, when you do this, have a glossary and use

it. What's this term? What's that term? On a separate basis. And then use it as an example. You might take perc as one, and you might take this as another.

If we were to have this statistical number, it would mean this. That definition gives us this number. I think it's important.

That's what we have got to face, and you will be facing the possibility that a different definition is what is ultimately used in the control process. Okay? All right. Fine. Now we're back until --

DR. FROINES: We are escalating the presentation before the ARB. We are escalating our presentation on a meaningful subject.

DR. BYRUS: I want to go back to 5-2, but I want to ask the question of the range of the five, and what's going to go on between now and the the next document, and that is what do you think is appropriate vis-a-vis the new comments that you have had from EPA and your familiarity with their draft document? And to what degree should they be incorporated into Table 5?

DR. FROINES: We could certainly put those in there and just cite those as it is.

DR. BYRUS: External review draft.

DR. FROINES: Excuse me. That's not the question I'm asking. The question I'm asking -- I understand that you could just do that, but I am saying give me your scientific judgment.

I want to continue discussion, assuming that it was in there, and talk about from a standpoint of the scientific validity of whether or not it's an issue of what you want.

DR. DAWSON: The difference between the EPA numbers -- I mentioned one. One is their use of not -- the absence of their use of the typical default scaling factor. So that would like put their number in the left-hand column.

And then the other thing that an EPA member would include would be they would have the a tissue-dose model based on the rat and then a tissue-dose model based on that plus the rat/extrapolation of the monkey.

DR. ALEXEEFF: In the analogy of the methylene chloride situation where we have the dosimetric adjustment for the animals in the study and then you have the species-to-species adjustment. As in this case, it's rat to monkey, where in the methylene chloride, we had rats -- or a mouse in vitro to human in vitro. It's a species adjustment factor.

DR. DAWSON: So the methylene chloride data available were not adequate to include the which decided to include the species-to-species as the best value.

DR. ALEXEEFF: Right. And we decided the same thing in this case.

DR. FROINES: Well, see if that's that's the case, then I think the document has a little bit of obscurity. I know you say it, but I think it needs to be more sharply done.

DR. ALEXEEFF: That's a good point. Okay. Now we're down -- I have mentioned about the cell proliferation and why the actual cell proliferation numbers are, in general, higher than the non -- but you see them on that bottom of the cell proliferation. There are several different models that one can assume when we had that slide up there.

Is it still up there? Yes, it is.

The proliferation effect can occur at different points of the process. You can proliferate normal, malignant, premalignant. You can proliferate the premalignant. You can proliferate the premalignant to malignant. There are different parts that can occur, different combinations.

What if you assumed it only proliferated this? What if you if assumed this portion of it? Or what if you assumed only these two? These are different combinations, why they have the different models, the different parts of this proliferation process, the total number of that are used.

But what happens is in the calculation, they end up reducing down to two possible proliferation choices in terms of actual numbers, and the lowest number -- which one is this?

DR. DAWSON: The one that had low risk?

DR. ALEXEEFF: Yes.

DR. DAWSON: The bottom left-hand corner.

DR. ALEXEEFF: That's this one?

DR. DAWSON: Yes.

DR. ALEXEEFF: This is the one with the lowest risk in the table. So in this case, the idea is it will only increase the proliferation rate here from the proliferation rate here, (indicating on slide) but not the proliferation rate directly within the cell. In other words, some -- we felt that that was the less likely of the cell proliferation if something was going to cause it. We don't think it would be so selective on those two slides, but it's possible.

And then the other thing is when you actually do the calculations using that model, it's just barely -- what's the correct statistical term? It's barely --

DR. DAWSON: Well, it's barely significant.

DR. ALEXEEFF: The choice of that model is -- in the extrapolation, it almost falls out of it being considered.

DR. DAWSON: A good fit.

DR. ALEXEEFF: The fit is barely justifiable, you know, in terms of it being a reasonable fit. So that's another issue with that particular data set.

Now, actually -- I'm done with the table.

I have these other comments from the Formaldehyde Institute I would be happy to go through that if you would like me to.

DR. GLANZ: Could I ask you one last question about this table and one thing that I had a hard time following? The different scaling factors. Could you just say a few words about

where these came from why you ended up picking the 1.2.

DR. ALEXEEFF: Well, 1.2 is the scaling factor which is suggested in our guidelines as a default scaling factor. That's a surface area scaling factor from rodent to human.

The No. 1, the "none" --

DR. GLANZ: Just to refresh my memory, what's built into that besides body surface area?

DR. DAWSON: Do you want me to finish? The idea of the scaling factor is that you're are trying to figure out what concentration gives you the same risk in animals. In that case you just take the assumption that the total intake rate over the body area gives you the same scaling, and you can justify it. Several different ways of justifying that.

DR. GLANZ: I think rodents are -- people are more than 1.2 times as big as rodents.

DR. DAWSON: Oh, yes, yes. Right.

DR. GLANZ: Isn't there other stuff built into that?

DR. ALEXEEFF: The 1.2 is 1.2 versus a 1. That is a very tricky point. In this case the 1 represents that a part per million to the rat is the same as a part per million to a human.

Now what is often -- for some of the compounds we have dealt with like chloroform, let's say, we didn't have inhalation data, and EPA often expresses its scaling factor on a milligram per kilogram basis. So if you assumed how much got in and then scaled from how much got in, it's a slightly different number

than 1.2 to clarify it.

In this case, it's 20 percent higher than if you assumed that what animals -- what rats breathe, humans breathe, the same amount.

DR. GLANZ: So this is in addition to the light scaling?

DR. DAWSON: It's just a strict body surface area.

DR. GLANZ: I would think it would be some very large number. People's have a larger body than rats.

DR. DAWSON: Well, remember, though, that the intake rate goes up as well. So what this is is the ratio of intake rate to surface area.

DR. GLANZ: So this is taking into account respiratory rate and all that kind of stuff. So this is saying that if you look at the respiratory rate times the tidal volume divided by the body surface area for rats and for people, and take the ratio, essentially all that stuff

DR. BECKER: Then if you apply the finding to the DNA and you use the monkey data you get the other equivalent.

DR. GLANZ: Well, that was what I was saying as to the complexity of this document, what happens is that the number is basically a five-fold difference. If you only look at the lung, I think the contact number was just for the lung, not systemic, just assuming that this is in the upper airways. And the far right column is only the monkeys. So that's only using the monkey data; is that correct?

DR. DAWSON: Well, that's essentially the general idea, but I just might add that what I call the generic contact factor is what should happen if everything -- if the metabolism is working the way it generally is supposed to; namely, that it's drawing two-thirds body weight. So if you put that stuff in there, then you get this contact scaling factor assuming that's just the surface layer that keeps out the binding rather than the whole body which is kind of a basis for the ultimate systemic scaling.

But then the monkeys come along, and they basically contradict the dosimetry for the monkeys, contradict that. Because it should be the other way around. The monkeys are better able to detoxify as would be predicted.

DR. BYRUS: But that's maybe because they didn't add up the total amount bound completely.

DR. DAWSON: Yes. Oh, yes. Sure. Right. And there are a lot of other things. They don't breathe through their noses, and they didn't get a big enough dose. Because if the monkeys were not breathing through their noses, then nine-tenths of it went around their noses. You would only accept one-tenth only to show up in the nose.

DR. ALEXEEFF: The interesting thing is if the monkeys were breathing the formaldehyde, and if it is irritating to them, did they switch from nose from to mouth breathing?

DR. DAWSON: They didn't sample the oral cavity.

DR. ALEXEEFF: That's right. They didn't sample the oral cavity at all. They sampled the rest of it. They found some, sure enough, down in the lungs. I'd like to say, that I hope this stuff is clarified.

DR. BYRUS: Why does EPA like that number? Aren't they aware of that?

DR. DAWSON: Well, I have talked to them about it a few times.

DR. BYRUS: What do they say?

DR. DAWSON: Well, they say that's a nice idea, but they don't understand it or whatever. But in defense of the EPA, if the monkeys were breathing entirely through their mouths and if -- well, you know, if you made a number of other assumptions and if nasal cancer is the only concern, which is what EPA is assuming, then this would make sense, and all the other assumptions about it.

DR. ALEXEEFF: I think that's one difference. Our -- the fundamental assumption is that we have is that formaldehyde does not restrict its cancer effects to the nasal epithelium just because that was what was shown in the rats.

There are a lot of examples of concordance between monkeys from one location to another is not decided. And for us it's a sort of logical sequence that if humans are going to be breathing through the mouth, they are not going to be getting cancer in the nose. They might get cancer in their nose process

as formaldehyde is a carcinogen.

The question is I think if you assume that what is happening in the mouse's nasal area is very peculiar to the rat. In other words -- excuse me. I said "mouse."

If what's happening in the rat's nasal area is peculiar to the rat; there is something happening in the rat's nasal area that is causing cancer, and it's not relevant to any other species. And that's the assumption they're making. You're going to prove it's in the epithelium and make the comparison with other species.

But our assumption is that formaldehyde is neotoxic, and it can cause cancer throughout the respiratory tract. And in rats it shows up in the epithelium. That's the difference in the approach.

And I think that's why there is that focus on the nasoepithelium and why we disagree with that assumption. That was the assumption presented by CIAC, and their staff feels it's a valid assumption. And we disagree.

DR. DAWSON: And also I may say that as in Cassanova, the ones that did the study, she says that she watched the monkeys at some time during their six hours, and one of them in particular didn't seem to be bothered by formaldehyde and didn't breathe through its mouth. And it was kind of anecdotal.

DR. ALEXEEFF: The other thing that I think really justifies our assumption there is the monkey cell proliferation

rate. Now, if we wanted to go the next step in the monkey, the monkey beyond would be -- we have got cell proliferation in the rat, but what about cell proliferation in the monkey, and how does that fit in?

The information that we have is that cell proliferation in the monkey occurs not just in the nasal epithelium, but in the larynx and the lower part of the lung. That would be what with we would consider to be the next step of consideration, but the question is you can always keep taking this further and further, and are we really improving the assessment or not?

But I think what it does do when we deal with it is what are the bounds of this risk number? We have made the assumption and where are we going to take it?

DR. FROINES: How many monkeys were there?

DR. DAWSON: Three.

CHAIRMAN PITTS: Could I interject just at this point? A couple of points at Part A, because they may be relevant in the discussion. And then we can come back. I'll make them fast.

I would like you to hear this, because I'm a little concerned about this, okay? And I hope from another perspective if we have this in December, I would hope some of these questions in Part A, we can get together and address these questions which are relevant, because could I just ask these quick questions about Part A?

One of them is I see here on page A 12 on Emissions from

Mobile Sources, and I see throughout the point that something like 90 percent of the formaldehyde in outside ambient air average over the state is a result of chemical oxidation, okay? That's reactions, and smog reactions, and so on.

But to have -- and that number of tons per day of formaldehyde is based on ARB mobile source emission data, right? And, in fact, the data, other data, are the 1984 studies from SAI or someone but they have emissions.

Well, it's noted on the bottom of page A 12 -- and this is quite -- I think as a result of the discussion we had, but actually the emissions data for reactive organic gasses from motor vehicles appear to be low by a factor of about anywhere from 200 to 400 percent. In other words, the numbers that you get by using the existing ARB or EPA mobile source models which tell you how many such coming out the tailpipe is clearly off by a factor of almost 300 percent.

MS. SHIROMA: Dr. Pitts, we worked closely with our --

CHAIRMAN PITTS: But that's at the bottom of page A 12 where you say, in fact, this is exactly the case. This is a change from the previous draft that you have.

But you are saying staff believes that a significant portion of the error is 50 to 100 percent off in terms of formaldehyde. Is that what you're saying?

MS. SHIROMA: That's right.

CHAIRMAN PITTS: So then what I'm asking is, given your

work where you got that, do the figures, the numbers, have you changed all the numbers and all the figures to reflect that you have a 50 to 100 percent change? Do you follow what I'm saying?

DR. BECKER: Yes.

CHAIRMAN PITTS: Let me say for the benefit of the people here it's pretty clear that the number is at least 50 or a hundred percent for total reactive organic gasses. I know it has to be exceeded. I would guess, then, that you're saying that your staff found maybe these numbers are wrong by a factor of two. You have to double them or something like that. Is that what you're saying?

DR. DAWSON: Yes, Dr. Pitts, actually we're just putting a kind of an error down by numbers. It would be 100 percent of the total rate to organic acid.

CHAIRMAN PITTS: You don't see the error bound in these figures.

DR. DAWSON: Right.

CHAIRMAN PITTS: You don't see the error bound in the numbers that I see of 90 percent, so many, 150,000 tons, whatever. Is that in those figures? I think that's something that could well be considered. I think it's important to consider and put in, refine the numbers that are in here that reflect the values that you actually have and are accepted by all involved in the game, all the atmospheric including the ARB, the problem being that the models that are used to predict what

comes out of the one's car are notoriously bad. They don't reflect actual driving method.

When you measure the atmosphere, you find out the measure of the level is at least a factor of two to four times higher than what you predict, and that's one point.

So is there any reason why this document shouldn't reflect it, and the error bars? If you've got error bars of 50 to 100 percent, that's a factor of two maybe. That's a lot better than error bars of a hundred back here from the biological side.

DR. DENTON: We will need to go back and talk to our Inventory Emissions Control people.

CHAIRMAN PITTS: To the Air Quality people and reconcile the two.

DR. DENTON: Exactly. Exactly.

CHAIRMAN PITTS: You have to reconcile the ones that we talked about to come out with what the numbers really are. Okay?

DR. DENTON: We will do our best.

CHAIRMAN PITTS: Okay. Well, that's important. We have two months now, a month and a half. I think it's important that we reflect this.

Because if one reads this paragraph -- I think it's in your own interest. You read a paragraph that says they are off by their own assessment by maybe a hundred percent, but we have

put the numbers in here that don't reflect that. That's not what you want to see happen.

DR. DENTON: We can clarify that.

CHAIRMAN PITTS: With an argument that you still haven't verified.

The second point -- and this is strictly -- second point here is I note that we say that we are not going to estimate -- no estimates were made for formaldehyde actual levels at hot spots. In other words, about everything else we have done up to date, we do a modeling run. We run a hot spot.

Didn't we have a hot spot model on spice around here for ethylene oxide? Remember the spice we used? We have got a hot spot.

I noticed that a very bald statement was made: We are not going to do this, and that will be done in the risk-management phase, but it seems to me up to now we have had some indication of what the emission should be by a refinery, we would have modeled it and if not modeled, measured something in there so we have some hot spots.

MS. SHIROMA: Yes, and we understand that. The history of what you're speaking on here as far as our previous documents go. Basically we are in the era of streamlining.

So we felt that in the granting of things, looking at the major sources of formaldehyde, realizing that much of it is from the chemical reaction, there are a few sources that could be hot

spots. We looked at the overall information that we thought was tending to substantiate the exposure to California. We felt that basically because we had moved to take data coming in on specific points, that basically when we do go through that data they are timed to the new-source analysis. It wasn't in the central component point for identification.

CHAIRMAN PITTS: In all the other previous -- toxics, we have looked at it. Is that a change that's due to streamlining? If it is, I'm concerned about it. That's next to a hot spot if it's a change. Because it's formaldehyde. Maybe the source is formaldehyde, and it's a new deal.

DR. DENTON: No, this is not the start of a new trend. One of the problems with formaldehyde is that a lot of it does come from mobile sources, and that takes a remodel. But that hasn't been remodeled yet. And so because of the sources, it came from a mobile source.

Because we knew that this data was going to be coming in from the 25, 28, we decided to go ahead with the document. But this is only unique to formaldehyde.

MS. SHIROMA: I'm sorry. I'm saying that first, formaldehyde is unique in terms of the overall emissions, in terms of the overall exposure, whether it's outdoor or indoor. And your point is well taken on that.

And we do not have a thorough analysis for a hot spot in this document. We felt that for the purposes of going through

your review and the Board's review it is not an essential component for the compound.

There will be other compounds coming before you where the situation will be similar, and where we can put the new-source analyses in, we will. This particular compound, we feel that if you look at the whole emissions inventory, there are a few sources. There may be hot spots. We felt at this point we should not delay to wait for that.

CHAIRMAN PITTS: You might also argue that that indoor was so high you might want to, in the little time you have, another six weeks, put something in there other than the bald statement that you will look at it. Maybe a little explanation along the lines I indicated. I think that again -- just so the public, you know, someone living near a refinery says, okay, it's coming out on such and such a site, feel a little left out of it.

The other thing is I noticed that we have on smoking here -- and Stan did not put me up to this. I mentioned it to him this morning. And he didn't even blink. He just grinned. On page A-47 here we have Lofroth. I can't pronounce his name. I know the guy. It's got an umlaut over the "o." But I can't pronounce an umlaut anyway. But that's okay.

On page A-47 in the middle of the paragraph it says,

(Reading)

Lofroth et al. recently measured formaldehyde

concentrations in sidestream cigarette smoke and determined the airborne yield per cigarette is two milligrams, or 2,000 micrograms.

(End of reading)

Okay. And it said they were -- the caveat that's under lab conditions.

And then it says (Reading)

Although cigarette smoke can elevate formaldehyde concentrations in small and closed spaces .... the average formaldehyde concentration of a home does not appear to be elevated significantly by the presence of smokers.

(End of reading)

Is that really true? Do you want to put the data in -- not put the data in because that's not going to show the actual concentration.

DR. DAWSON: Yes, we found that true. The elevations actually for cigarette smoke indoors do not significantly affect the overall concentration.

CHAIRMAN PITTS: How much would it go? One ppbv or two? Is that what you're saying?

DR. DAWSON: Well, maybe a ppbv -- of the total concentration, it might be give 55 or 59 ppbv.

CHAIRMAN PITTS: So it might go five or nine. But you see that's more than the average outdoor. But the increase, I

could say, then, that the smoking indoors increases your risk in the same degree, if I assume linearity, as just going outside on a smoggy day in L.A; is that right? Just smoking increment.

DR. DAWSON: I realize what you're saying. That was just based on the one study. That was the SAI study which was fairly insignificant. They only studied three homes which mentioned in part of their survey that they had smokers in their home. So out of that extrapolation they correspond the concentration of the 59 ppbv with the indoor mean concentration of a ppbv of over 70. So it wasn't conclusive. That study wasn't conclusive in saying that okay, cigarette smoke in general is going to contribute nine ppbv.

CHAIRMAN PITTS: No, I understand. But you could conclude that that's not totally insignificant.

DR. DAWSON: Right.

DR. GLANZ: I would agree. I was busy struggling with Part B. I figured you would take Part A. I think that's a very misleading statement that you have in there, actually, for several reasons.

Isn't there -- I could have sworn that I have seen measurements of formaldehyde in indoor environments when people are smoking. I think there is older stuff that people have put down.

DR. DENTON: Dr. Glanz, the reason for that statement is there was not significant difference in those homes, and I would

point out there were only three homes that were studied. So the significance refers to the statistical.

DR. GLANZ: Yes, that's very misleading especially with the angles free.

DR. DAWSON: The Hawthorne et al; Traynor study, those studies did not study the cigarette smoke. And it was shown that that was still indoor concentrations.

CHAIRMAN PITTS: Although cigarette smoke and elevated formaldehyde concentrations in small enclosed spaces like external chambers, how small are external chambers?

DR. DAWSON: I'm not sure.

CHAIRMAN PITTS: Well, that's important. You see, if you get a little more information on that end, you're a little better off than stating the facts, and maybe the reader can sort of draw the conclusion.

In three homes, certainly not a statistical number, however, the following was found. These chambers are this big, and if you have more people in this, and you get into a small den, you line up -- and something like that.

DR. GLANZ: I'm amazed that somebody does statistics with this sample size. You probably have a right to about a one percent power.

CHAIRMAN PITTS: Well, we have some other things we can discuss. I think in fairness to our --

DR. FROINES: Before we stop, can I ask George a

question, or anybody who knows the answer. I don't know the answer. Does anybody have any idea if you live in Los Angeles, say, and it's a hot, smoggy August day, does anybody have any idea how much -- has anybody ever looked at cell proliferation under those kinds of environments?

DR. DAWSON: I haven't heard of anything, have you?

DR. ALEXEEF: No, I haven't.

DR. FROINES: Hasn't somebody put a rat in L.A. air and tried to see if it --

DR. ALEXEEF: Sounds like a good idea for a grant.

CHAIRMAN PITTS: Could you say that for the benefit of the audience?

DR. WITSCHI: Once many, many years ago, 20 years ago, I talked to a man who at one time in Montreal made headlines by publishing evidence that lung cells were renewing. Until then the lung had been considered to be an organ that there was no cell renewal.

And I called him, and he just chuckled, and he said, from the moment he kept his rats in clean environments, he didn't see any cell turnover in the lungs anymore. So I don't think really that cell turnover in the lungs was finished then.

DR. DAWSON: Well, actually, I do know of one study, at least, by Russ Sherwin at USC who took -- I think it was mice -- and had them in clean air, really filtered the air well. And then he had just ordinary L.A. air. And there were very

significant effects. One I'm certain of was adenoma.

DR. FROINES: Well, sometime when George and you guys don't have anything else to do, maybe you ought to try and model what that would look like in terms of risk, because that's real.

DR. WITSCHI: I'll tell you another one. I just finished a study in which I treated a bunch of hamsters in lung specific carginogen. A couple of the guys were kept in air, about 30 percent with are come in lung. Had exposed 24 hours a day to 50 ppm for six months, and none of them had any lung tumors. So it's good for you.

CHAIRMAN PITTS: Well, that's it for today.

(The meeting was adjourned at 11:55 a.m.)

--o0o--

CERTIFICATE OF SHORTHAND REPORTER

I, CLARA MAE MATHIS, a Certified Shorthand Reporter of the State of California, do hereby certify:

That I am a disinterested person herein; that the foregoing meeting of the Scientific Review Panel of the Air Resources Board was reported in shorthand by me, Clara Mae Mathis, and thereafter transcribed into typewriting.

I further certify that I am not of counsel or attorney for any of the parties to said meeting nor in any way interested in the outcome of said meeting.

IN WITNESS WHEREOF, I have hereunto set my hand this 6th day of November, 1991.

CLARA MAE MATHIS
CSR No. 2832